

AMENDMENTSIn the Claims

- 1.(canceled)
- 2.(canceled)
- 3.(canceled)
- 4.(canceled)
- 5.(canceled)
- 6.(canceled)
- 7.(canceled)
- 8.(canceled)
- 9.(canceled)

1 10.(previously presented) A composition comprising a polymerizing agent including a molecular
2 tag covalently bonded to a site on the polymerizing agent and a monomer including a molecular tag,
3 where at least one of the tags has a fluorescence property that undergoes a change before, during
4 and/or after each of a sequence of monomer incorporations due to an interaction between the
5 polymerizing agent tag and the monomer tag.

1 11.(canceled)
2 12.(canceled)

1 13.(previously presented) The composition of claim 10, wherein the polymerizing agent is a
2 polymerase or reverse transcriptase.

1 14.(previously presented) The composition of claim 13, wherein the polymerase is selected from
2 the group consisting of *Taq* DNA polymerase I, T7 DNA polymerase, Sequenase, and the Klenow
3 fragment from *E. coli* DNA polymerase I.

1 15.(previously presented) The composition of claim 13, wherein the reverse transcriptase
2 comprises HIV-1 reverse transcriptase.

1 16.(previously presented) The composition of claim 10, wherein each of the monomers
2 comprises a deoxynucleotide triphosphate (dNTP) and the monomer tag is covalently bonded to the
3 β or γ phosphate group of each dNTP.

1 17.(previously presented) The composition of claim 10, wherein the tags comprise fluorescent
2 tags and the fluorescence property comprises an intensity and/or frequency of emitted fluorescent
3 light.

1 18.(previously presented) The composition of claim 17, wherein the fluorescence property is
2 fluorescence resonance energy transfer (FRET) where either the monomer tag or the polymerase tag
3 comprises a donor and the other tag comprises an acceptor and where FRET occurs when the two
4 tags are in close proximity.

5 19.(previously presented) The composition of claim 14, wherein the polymerase comprises *Taq*
6 DNA polymerase I having a tag attached to an amino acid at a specific amino acid position of the
7 *Taq* DNA polymerase I, where the amino acid position is selected from the group consisting of 513-
8 518, 643, 647, 649 and 653-661 of SEQ. ID No. 11, where the tag comprises a fluorescent molecule.

20.(canceled)

21.(canceled)

22.(canceled)

22.(canceled)

23.(canceled)

24.(canceled)

1 25.(withdrawn) A single molecule sequencing apparatus comprising a substrate having a first
2 chamber in which at least one tagged polymerase is confined therein and a second chamber including
3 tagged dNTPs and a channel interconnecting the chambers, where a detectable property of at least
4 one tag undergoes a detectable change during a monomer incorporation cycle.

1 26.(withdrawn) The apparatus of claims 24, further comprising a plurality of monomer
2 chambers, one for each tagged dNTP.

1 27.(withdrawn) A mutant Taq polymerase comprising native Taq polymerase with a cysteine
2 residue replacement at a site selected from the group consisting of 513-518, 643, 647, 649 and 653-
3 661 and mixtures or combinations thereof.

1 28.(withdrawn) The polymerase of claim 27, wherein the cysteine residue includes a tag
2 covalently bonded thereto through the SH group.

1 29.(withdrawn) A system for retrieving stored information comprising:
2 a unknown nucleotide sequence representing a data stream;
3 a single-molecule sequencer including a polymerase having a tag associated therewith and
4 monomers for the polymerase, each monomer having a tag associated therewith;
5 an excitation source adapted to excite the at least one of the tags; and
6 a detector adapted to detect a response from at least one of the tag,
7 where the response changes during polymerization of a complementary sequence and the
8 changes in response represent a content of the data stream.

1 30.(withdrawn) A system for determining sequence information from a single molecule
2 comprising:
3 a unknown nucleotide sequence;
4 a single-molecule sequencer comprising a polymerase having a tag associated therewith and
5 monomers for the polymerase, each monomer having a tag associated therewith;
6 a excitation source adapted to excite at least one of the tags; and
7 a detector adapted to detect a response from at least one of the tags,
8 where the response changes during polymerization of a complementary sequence and the
9 changes in the response represent the identity of each nucleotide in the unknown sequence.

1 31.(withdrawn) A method for sequencing a molecular sequence comprising:
2 supplying an unknown sequence of nucleotides or nucleotide analogs to a single-molecule

3 sequencer comprising a polymerase having a fluorescent donor covalently attached thereto and
4 monomers for the polymerase, each monomer having a unique fluorescent acceptor covalently
5 bonded to the beta or gamma phosphate thereof;

6 exciting the fluorescent donor with a light from an excitation light source;

7 detecting emitted fluorescent light from the acceptor during a monomer incorporation cycle
8 via a fluorescent light detector, where an intensity and/or frequency of the emitted light for the
9 incorporating acceptors changes during each monomer incorporation cycle; and

10 converting the changes into an identity of each nucleotide or nucleotide analog in the
11 unknown sequence.

1 32.(withdrawn) A method of sequencing an individual nucleic acid molecule or numerous
2 individual molecules in parallel including the steps of:

3 immobilizing a member of the replication complex comprising a polymerase including a tag
4 attached thereto, a primer or a template sufficiently spaced apart to allow resolution detection of each
5 complex on a solid support;

6 incubating the replication complex with cooperatively-tagged nucleotides, each nucleotide
7 including a unique tag at its gamma-phosphate, where each nucleotide can be individually detected;

8 detecting each nucleotide incorporated by the polymerase as the polymerase transitions
9 between its open and closed form, which causes a change in a detectable property of at least one of
10 the tags or as the pyrophosphate group is released by the polymerase; and

11 relating the changes in the detectable property to the sequence of nucleotides in an unknown
12 nucleic acid sequence.

1 33.(withdrawn) A γ -phosphate modified nucleoside comprising γ -phosphate modified dATP,
2 dCTP, dGTP and dTTP.

1 34.(withdrawn) A primer sequence or portion thereof selected from the group consisting of
2 Sequence 1 through 29.

35.(canceled)

36.(canceled)

37.(canceled)

38.(canceled)

39.(canceled)

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41.(canceled)

42.(canceled)

43.(canceled)

44.(canceled)

45.(canceled)

46.(canceled)

47.(canceled)

48.(canceled)

1 49.(canceled)

1 50.(currently amended) A composition comprising a polymerizing agent including a molecular
2 tag covalently bonded to a site on the polymerizing agent and a deoxynucleotide triphosphate (dNTP)
3 including a molecular tag covalently bonded to the β or γ phosphate group of the dNTP, where at
4 least one of the tags has a fluorescence property that undergoes a change before, during and/or after
5 each of a sequence of monomer incorporations due to an interaction between the polymerizing agent
6 tag and the monomer dNTP tag.

1 51.(previously presented) The composition of claim 50, wherein the polymerizing agent is a
2 polymerase or reverse transcriptase.

1 52.(previously presented) The composition of claim 51, wherein the polymerase is selected from
2 the group consisting of *Taq* DNA polymerase I, T7 DNA polymerase, Sequenase, and the Klenow
3 fragment from *E. coli* DNA polymerase I.

1 53.(previously presented) The composition of claim 51, wherein the reverse transcriptase
2 comprises HIV-1 reverse transcriptase.

1 **54.(previously presented)** The composition of claim 50, wherein the tags comprise fluorescent
2 tags and the fluorescence property comprises an intensity and/or frequency of emitted fluorescent
3 light.

1 **55.(previously presented)** The composition of claim 54, wherein the fluorescence property is
2 fluorescence resonance energy transfer (FRET) where either the monomer tag or the polymerase tag
3 comprises a donor and the other tag comprises an acceptor and where FRET occurs when the two
4 tags are in close proximity.

5 **56.(previously presented)** The composition of claim 52, wherein the polymerase comprises *Taq*
6 DNA polymerase I having a tag attached to an amino acid at a specific amino acid position of the
7 *Taq* DNA polymerase I, where the amino acid position is selected from the group consisting of 513-
8 518, 643, 647, 649 and 653-661 of SEQ. ID No. 11, where the tag comprises a fluorescent molecule.